

What is claimed is:

1. An antisense molecule targeted to a nucleic acid molecule encoding human APPL, wherein said antisense molecule is complementary to an expression controlling sequence of said APPL encoding nucleic acid molecule, and upon binding to said APPL nucleic acid inhibits expression of APPL protein.
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- 10 2. The antisense molecule of claim 1 which is an antisense oligonucleotide.
- 15 3. The antisense oligonucleotide of claim 2 selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 4.
- 20 4. The antisense oligonucleotide of claim 3 having the sequence of SEQ ID NO:1, which is 5' - TCCCCGGCATCGTGGCGG - 3'.
- 25 5. The antisense oligonucleotide of claim 3 having the sequence of SEQ ID NO: 2, which is 5' - GACCTTGTCTGCAGGGC - 3'.
- 30 6. The antisense oligonucleotide of claim 3 having the sequence of SEQ ID NO: 4, which is 5' - GGGCAGCTTGTGATCCCCGGCATCGTGGCGG - 3'.
- 35 7. The antisense oligonucleotide of claim 2, wherein said antisense oligonucleotide induces apoptotic cell death in human cells.
8. The antisense oligonucleotide of claim 2, wherein said antisense oligonucleotide comprises at least one modified internucleoside linkage.

9. The antisense oligonucleotide of claim 8,
wherein said modified internucleoside linkage is a
phosphorothioate linkage.

5 10. The antisense oligonucleotide of claim 2,
wherein said antisense oligonucleotide comprises at least
one modified sugar moiety.

10 11. The antisense oligonucleotide of claim 10,
wherein said modified sugar moiety is a 2'-O-
methyloxymethyl sugar moiety;

15 12. The antisense oligonucleotide of claim 2,
wherein said antisense oligonucleotide comprises at least
one modified base.

13. The antisense oligonucleotide of claim 12,
wherein said modified base is a 5-methylcytosine.

20 14. A method of modulating the expression of APPL
in human cells or tissues comprising contacting said
cells or tissues with the antisense molecule of claim 1
in an amount sufficient to inhibit expression of APPL.

25 15. A method for controlling the expression of APPL
in human cells, said method comprising:

30 a) providing an antisense oligonucleotide
selected from the group consisting of SEQ ID NO: 1, SEQ
ID NO: 2 or SEQ ID NO: 4, which hybridizes to an
expression-controlling sequence of a nucleic acid
molecule that encodes APPL; and

35 b) administering said antisense oligonucleotide
to said human cells in an amount sufficient to control
expression of said APPL, whereby said antisense
oligonucleotide enters said cells expressing APPL and

5 binds specifically to the expression-controlling sequence
of said nucleic acid molecule encoding APPL thereby
inhibiting APPL expression.

10 5 16. The method according to claim 15, wherein said
human cells are selected from the group consisting of
skeletal muscle, heart, ovary, and pancreas.

15 10 17. The method according to claim 15, wherein
administration of said antisense oligonucleotide induces
apoptotic cell death in said human cell.

15 18. The method according to claim 15, wherein said
antisense oligonucleotide is an antisense oligonucleotide
analog.

20 19. The antisense oligonucleotide of claim 2,
wherein said antisense oligonucleotide is encoded by DNA.

20 20. A vector comprising the DNA which encodes the
antisense oligonucleotide of claim 19.

25 21. A method of treatment for human malignancy due
to the expression of an aberrant APPL protein in a
patient requiring such treatment, said method comprising
delivery of an antisense oligonucleotide of claim 3 in an
amount sufficient to control expression of said protein.

30 22. The method of claim 21, further comprising
administration of at least one additional anti-cancer
agent selected from the group consisting of cisplatin,
carboplatin, herceptin, taxol, taxane derivatives,
cyclophosphamide, methotrexate, vincristin, and
etoposide.

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23. A pharmaceutical preparation for treating human malignancy due to the expression by cells of an aberrant APPL protein, comprising an antisense APPL oligonucleotide in a biologically compatible medium.

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24. A pharmaceutical preparation according to claim 23, wherein said antisense oligonucleotide comprises the sequence of SEQ ID NO:1, which is 5' - TCCCCGGCATCGTGGCGG - 3'.

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25. A pharmaceutical preparation according to claim 23, wherein said antisense oligonucleotide comprises the sequence of SEQ ID NO:2, which is 5' - GACCTTGTCTGCGGGC - 3'.

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26. A pharmaceutical preparation according to claim 23, wherein said antisense oligonucleotide comprises the sequence of SEQ ID NO:4, which is 5' - GGGCAGCTTGTGATCCCCGGCATCGTGGCGG - 3'.

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27. A pharmaceutical preparation according to claim 23, which further comprises at least one targeting agent for improving delivery of said antisense oligonucleotide to said cells expressing said protein.

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28. A pharmaceutical preparation according to claim 27, wherein said at least one targeting agent comprises a lipid.

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29. A pharmaceutical preparation according to claim 23, wherein said antisense oligonucleotide is encapsulated in a lipid vesicle.

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30. The pharmaceutical preparation according to claim 23, wherein said antisense oligonucleotide is

selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 4, and is an analog having a modified internucleotide linkage.

5 31. The pharmaceutical preparation of claim 30, further comprising at least one additional anti cancer agent.

10 32. The pharmaceutical preparation of claim 31, wherein said anti-cancer agent is selected from the group consisting of cisplatin, carboplatin, herceptin, taxol, taxane derivatives, cyclophosphamide, methotrexate, vincristin, and etoposide.

15 33. The pharmaceutical preparation of claim 23, wherein said antisense APPL oligonucleotide is encoded in a vector.

20 34. A double stranded RNA molecule targeted to a nucleic acid molecule encoding human APPL, wherein said double stranded RNA molecule inhibits expression of APPL protein upon entry into a cell comprising APPL encoding nucleic acids.

25 35. The double stranded RNA molecule of claim 34, wherein said double stranded RNA molecule is an siRNA.

30 36. The double stranded RNA molecule of claim 34, wherein said double stranded RNA molecule is an shRNA.

37. An siRNA molecule as claimed in claim 35, having the sequence of SEQ ID NO: 6.

35 38. An shRNA molecule as claimed in claim 36, having the sequence of SEQ ID NO: 8.

39. A method of modulating the expression of APPL in human cells or tissues comprising contacting said cells or tissues with the siRNA molecule of claim 35 in 5 an amount sufficient to inhibit expression of APPL.

40. A method of modulating the expression of APPL in human cells or tissues comprising contacting said cells or tissues with the shRNA molecule of claim 36 in 10 an amount sufficient to inhibit expression of APPL.

41. A method for controlling the expression of APPL in human cells, said method comprising:
15 a) providing a siRNA molecule of SEQ ID NO: 6; and

20 b) administering said siRNA molecule to said humans cells in an amount sufficient to control expression of said APPL, whereby said siRNA molecule enters said cells expressing APPL and inhibits APPL expression.

42. The method according to claim 41, wherein said human cells are selected from the group consisting of skeletal muscle, heart, ovary, and pancreas.

25 43. A method for controlling the expression of APPL in human cells, said method comprising:
a) providing a shRNA molecule of SEQ ID NO: 8; and

30 b) administering said siRNA molecule to said humans cells in an amount sufficient to control expression of said APPL, whereby said siRNA molecule enters said cells expressing APPL and inhibits APPL expression.

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44. The method according to claim 43, wherein said human cells are selected from the group consisting of skeletal muscle, heart, ovary, and pancreas.

5 45. A method for controlling the expression of APPL in human cells, said method comprising:

a) providing a vector encoding an siRNA molecule of SEQ ID NO: 6; and

10 b) administering said vector to said humans cells in an amount sufficient to control expression of said APPL, whereby said vector enters said cells expressing APPL and inhibits APPL expression.

15 46. The method according to claim 45, wherein said human cells are selected from the group consisting of skeletal muscle, heart, ovary, and pancreas.

20 47. A method for controlling the expression of APPL in human cells, said method comprising:

a) providing a vector encoding an shRNA molecule of SEQ ID NO: 8; and

25 b) administering said vector to said humans cells in an amount sufficient to control expression of said APPL, whereby said vector enters said cells expressing APPL and inhibits APPL expression.

30 48. The method according to claim 47, wherein said human cells are selected from the group consisting of skeletal muscle, heart, ovary, and pancreas.

35 49. A method of treatment for human malignancy due to the expression of an aberrant APPL protein in a patient requiring such treatment, said method comprising delivery of a siRNA molecule of claim 35 in an amount sufficient to control expression of said protein.

50. The method of claim 49, further comprising administration of at least one additional anti-cancer agent selected from the group consisting of cisplatin, carboplatin, herceptin, taxol, taxane derivatives, 5 cyclophosphamide, methotrexate, vincristin, and etoposide.

10 51. A method of treatment for human malignancy due to the expression of an aberrant APPL protein in a patient requiring such treatment, said method comprising delivery of a shRNA molecule of claim 36 in an amount sufficient to control expression of said protein.

15 52. The method of claim 51, further comprising administration of at least one additional anti-cancer agent selected from the group consisting of cisplatin, carboplatin, herceptin, taxol, taxane derivatives, cyclophosphamide, methotrexate, vincristin, and etoposide.

20 53. A pharmaceutical preparation for treating human malignancy due to the expression by cells of an aberrant APPL protein, comprising an APPL siRNA in a biologically compatible medium.

25 54. The pharmaceutical preparation according to claim 53, wherein said siRNA comprises the sequence of SEQ ID NO:6.

30 55. The pharmaceutical preparation according to claim 54, which further comprises at least one targeting agent for improving delivery of said siRNA to said cells expressing said protein.

56. The pharmaceutical preparation according to
claim 55, wherein said at least one targeting agent
comprises a lipid.

5 57. The pharmaceutical preparation according to
claim 56, wherein said siRNA is encapsulated in a lipid
vesicle.

10 58. The pharmaceutical preparation of claim 54,
further comprising at least one additional anti cancer
agent.

15 59. The pharmaceutical preparation of claim 58,
wherein said anti-cancer agent is selected from the group
consisting of cisplatin, carboplatin, herceptin, taxol,
taxane derivatives, cyclophosphamide, methotrexate,
vincristin, and etoposide.

20 60. The pharmaceutical preparation of claim 53,
wherein said siRNA is encoded in a vector.

25 61. A pharmaceutical preparation for treating human
malignancy due to the expression by cells of an aberrant
APPL protein, comprising an APPL shRNA in a biologically
compatible medium.

30 62. The pharmaceutical preparation according to
claim 61, wherein said shRNA comprises the sequence of
SEQ ID NO: 8.

35 63. The pharmaceutical preparation according to
claim 62, which further comprises at least one targeting
agent for improving delivery of said shRNA to said cells
expressing said protein.

64. The pharmaceutical preparation according to
claim 63, wherein said at least one targeting agent
comprises a lipid.

5 65. The pharmaceutical preparation according to
claim 64, wherein said shRNA is encapsulated in a lipid
vesicle.

10 66. The pharmaceutical preparation of claim 61,
further comprising at least one additional anti cancer
agent.

15 67. The pharmaceutical preparation of claim 66,
wherein said anti-cancer agent is selected from the group
consisting of cisplatin, carboplatin, herceptin, taxol,
taxane derivatives, cyclophosphamide, methotrexate,
vincristin, and etoposide.

20 68. The pharmaceutical preparation of claim 61,
wherein said shRNA is encoded in a vector.